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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,607	10/23/2001	Lino Tavares	208.1004US	1029

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EXAMINER	
GHALI, ISIS A D	
ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/045,607	TAVARES ET AL.	
	Examiner	Art Unit	
	Isis A. Ghali	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-11,13,14,16,20,22-24,29,30,32-38 and 40-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11,13,14,16,20, 22-24,29,30,32-38 and 40-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' amendment and request for RCE, both filed 11/02/2007.

Claims 8-11, 13, 14, 16, 20, 22-24, 29, 30, 32-28, and 40-49 are pending and included in the prosecution.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/02/2007 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 8-11, 13, 14, 16, 20-24, 29, 30, 32-38, and 40-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,910,205 ('205) combined with US 5,968,547 ('547).

> The present claims 8-11, 13, 14, 16 and 47 are directed to method of treating seasonal allergy or chronic urticaria comprising administering to the patient a transdermal delivery system containing loratadine, and the claims recite broad plasma levels and release rates as implied by the term "about". Claims 20-24, 29, 30, 32-38, 45 and 48 are directed to transdermal delivery system containing loratadine and provide broad plasma levels and release rates as implied by the term "about". Claims 46 and 49 are directed to method of treating seasonal allergy or chronic urticaria comprising administering to the patient a transdermal delivery system containing loratadine wherein the device comprises reservoir layer consisting essentially of 20-90% polymer, 0.1-30% softening agent, 0.1-20% loratadine and 0.1-30% solvent, and the claims recite broad plasma levels and release rates as implied by the term "about".

US '205 teaches a transdermal delivery system of loratadine for the treatment of allergic conditions (abstract). The system is formed of patch applied to skin for a specific

period of time to permit the penetration of a desired amount of loratadine through the skin. The patch will be worn from one to four days and provides a total daily dose of 0.5 to 5 mg (col.2, lines 28-34). The patch comprises a reservoir having 10-20% loratadine; 50-60% solvent; and 20-35% fatty acid esters, i.e. softening agents (col.2, lines 19-29). The patch further comprises a backing layer and a release liner (col.2, line 64; col.3, line 6). The patch delivers 0.66 mg/15 cm^2/day of loratadine for the formulation comprising loratadine, solvent and skin softener (Table I). The reference disclosed that the dose may be varied depending on the size and age of the patient, and may also depend upon the severity of the condition being treated (col.3, lines 56-60). The frequency of dosage application can be once every 3 days to once every 7 days (col.4, lines 5-10). The claimed delivery rates are met by the reference because the claimed rates are broadened by the term "about" and inclusive of the rates disclosed by the prior art. The prior art rate of delivery is 0.66 mg/15 cm^2/day, i.e. 44 µg/cm^2/day, and as claimed is about 16.2 µg/cm^2/day.

Additionally, the claimed release rates are determined by Valia-Chein cell, and the prior art is silent regarding the test method and the art does not appear to rely on, or teach the test method. The Patent Office is not equipped with test facilities for result testing. Hence, the instantly claimed release rates are met by the prior art.

The reference does not teach the specific delivery profile of loratadine, the specific amounts of different ingredients, or specific structure and formulation of a transdermal device including specific polymer, specific solvents and specific softening agents in the transdermal delivery system.

US '547 teaches a transdermal drug delivery device for controlled delivery of drug for 3 days and maintaining the delivery for additional 2 days in accordance to the zero order kinetic of the drug (abstract). When the drug applied transdermally, it follows the pharmacokinetics to provide its effect over prolonged period (col.4, lines 42-67, col. 5, lines 1-8). The device comprises backing layer, polymeric reservoir and protective liner (col.20, lines 17-27). The reservoir comprising: 1-90% of polymeric material, 0.1-30% of the drug, 0.1-30% softener, and 0.1-30% of solvent (col.20, lines 55-60). The polymeric material of the reservoir is pressure sensitive adhesive and contains rubber, silicone or block-copolymers (col.18, lines 55-65). The solvents used include those contain at least one acidic group, particularly, monoesters of dicarboxylic acids, such as monomethyl glutarate and monomethyl adipate (col.20, lines 5-10). The softeners include medium chain triglycerides of the caprylic/capric acids or coconut oil, undecanol, octanol, and dodecanol (col.19, lines 58-68). The backing is laminate of polymer and aluminum foil (col.18, lines 25-30).

It is evident from the disclosure of US '547 that when the drug is included in the described transdermal device, the drug follows and is delivered according to its pharmacokinetics for period of 5 days as desired by applicants. The structure and formulation of the reservoir of the present transdermal device are identical to that of US '547. Applicants disclosed on the paragraph bridging page 23 and 24 that the pharmacokinetic information for oral loratadine is available in the literature and a release rate for a loratadine transdermal delivery system was calculated from the available data. Applicants also admit on page 24, first full paragraph that any type of

transdermal delivery system may be used in accordance with the methods of the present invention so long as the desired pharmacokinetic are attained over at least 3 days to about 8 days.

Therefore, having available within hands the disclosure of US '205 that teaches loratadine delivered transdermally from formulation comprising solvent and softener, and US '547 that teaches drug delivery rate over 3-5 days following the pharmacokinetics of the drug and is attained by specific structure and formulation of a transdermal drug delivery system, along with the known pharmacokinetics of loratadine, one having ordinary skill in the art at the time of the invention would have designed transdermal drug delivery device to deliver loratadine as disclosed by US '205 and use the device disclosed by US '547 and would calculate the transdermal release rates from the available pharmacokinetic data of loratadine to achieve a transdermal delivery device having the structure and reservoir formulation comprising loratadine, polymer, softener selected from medium chain triglycerides of the caprylic/capric acids or coconut oil, undecanol, octanol, and dodecanol, and solvent selected from one of monoesters of dicarboxylic acids, wherein the device delivers loratadine at a delivery rate in accordance to its pharmacokinetics to treat patients suffering from allergic reactions with great success.

The determination of the relative release rate via an in-vitro permeation test utilizing a Valia-Chien cell is known in the art and it is not part of the claimed method of treating allergic rhinitis; or even a part of the transdermal device that provide particular plasma levels of loratadine. It is only an in-vitro diagnostic test that is expected to

provide the same results obtained from two similar delivery devices tested under the same circumstances, and the recitation of this in-vitro test does not impart patentability to claims directed to method of treating allergic rhinitis or claims directed to transdermal device applied to patients to provide specific plasma levels of loratadine, i.e. in vivo use.

Response to Arguments

5. Applicant's arguments filed 10/02/2006 have been fully considered but they are not persuasive. Applicants traverse this rejection by arguing that:

1) Applicants argue that the independent claims as amended are patentably differentiated over the combination of Kogan and Reder.

In response to this argument, it is noted that the specific solvents and specific softener recites by currently amended claims are all disclosed by the Reder, and therefore, the combination of the references would teach including such agents in transdermal formulation.

2) Applicants argue it is improper to combine the Kogan patent that is directed to treatment of allergies by administering loratadine with Reder patent that is directed to treatment of pain by administering buprenorphine. Loratadine is structurally different from and have different effect in the body from buprenorphine. Examiner has not articulate the rationale of what would have prompted one having ordinary skill in the art looking to improve on formulation for treatment of allergies to look on a reference concerned with treatment of pain. Therefore, no prima facie case of obviousness has been established.

In response to this argument, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Loratadine was known at the time of the invention to be administered transdermally as disclosed by Kogan. Reder taught that when the drug is included in the described transdermal device, the drug follows and is delivered according to its pharmacokinetics for period of 5 days as desired by applicants. Applicants disclosed on the paragraph bridging page 23 and 24 that the pharmacokinetic information for oral loratadine is available in the literature and a release rate for a loratadine transdermal delivery system was calculated from the available data. Applicants also admit on page 24, first full paragraph that any type of transdermal delivery system may be used in accordance with the methods of the present invention so long as the desired pharmacokinetic are attained over at least 3 days to about 8 days. Therefore, one having ordinary skill in the art at the time of the invention would have designed transdermal drug delivery device to deliver loratadine as disclosed by Kogan and use the device disclosed by Reder and would calculate the transdermal release rates from the available pharmacokinetic data of loratadine to achieve a transdermal delivery device having the structure and reservoir formulation comprising polymer, softener, solvent and loratadine that delivers loratadine at a delivery rate in accordance to its pharmacokinetics to treat patients suffering from

allergic reactions with great success. It has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir.1992). In this case, the cited prior art in the field of applicant's endeavor since both Kogan and Reder are concerned about transdermal delivery of active agents over 3-5 days following the pharmacokinetics of the drug that is attained by specific structure and formulation of a transdermal drug delivery system, and their combination is reasonable as stated above. The invention as a whole is taught by the combination of the references; therefore, prima facie case of obviousness has been established in the meaning of USC 103 (a).

> 3) Applicants argue that even if the references to be combined, the combination of the Kogan patent and the Reder patent would not replicate the claimed invention
>
> a) Applicants argue that buprenorphine, the active ingredient of the Reder patent is excluded from the scope of the present claims. Applicants argue that independent claims 8, 20 and 46 all recite that the active agent is limited to loratadine and the formulations and methods of the Reder patent all contain buprenorphine as a necessary ingredient and independent claims 8, 20 and 46 all recite that the active agent is solely limited to loratadine. Therefore, looking as the Reder reference as a whole, it is impermissible for the Examiner to "pick and choose" specific ingredients from the Reder patent to combine with the Kogan patent, without considering the entire teachings of the reference.

In response to this argument, it is established that in considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the

reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972). Kogan teaches loratadine administered transdermally and it is evident from the disclosure of Reder that when the drug is included in the described transdermal device, the drug follows and is delivered according to its pharmacokinetics for period of 5 days as desired by applicants. The structure and formulation of the reservoir of the present transdermal device are identical to that of US '547. Applicants disclosed on the paragraph bridging page 23 and 24 that the pharmacokinetic information for oral loratadine is available in the literature and a release rate for a loratadine transdermal delivery system was calculated from the available data. Applicants also admit on page 24, first full paragraph that any type of transdermal delivery system may be used in accordance with the methods of the present invention so long as the desired pharmacokinetic are attained over at least 3 days to about 8 days. It has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and

yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int 'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.*, 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions."

b. Applicants further submit that the neither Kogan nor Reder, or their combination teach or suggest the specific delivery profiles of loratadine as claimed in independent claims 8, 20 and 46.

In response to this argument, and upon careful review to Kogan reference, it is noticed that flux rate ranges from 6 μg/cm^2/day to 58 μg/cm^2/day that the release rate disclosed by Kogan obviates the claimed delivery rates because the delivery rate disclosed by Kogan is 44 μg/cm^2/day and the claimed delivery rate has lower range from 2 to 16.2 μg/cm^2/hr which is equivalent to 48 to 389 μg/cm^2/day. Therefore, the claimed delivery rates are met by the reference because the claimed rates overlapped with the rates disclosed by the reference.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

IG

/Isis A Ghali/
Primary Examiner, Art Unit 1611